

crying.<sup>8</sup> Nevertheless, they are rarely so large and certainly never as prolonged as those seen in smothering. They do not occur during sleep. Secondly, at about one minute after the onset of the episode there was a series of large breaths occurring at a relatively slow rate with a characteristically prolonged expiratory phase. This "gasping" respiratory pattern is a typical response to severe arterial hypoxaemia.<sup>10</sup> Thirdly, the episode was associated with a severe degree of sinus tachycardia.

Finally, some 60 seconds after the onset of the episode, there were the large slow waves and a subsequent isoelectric baseline on the electroencephalogram typical of cerebral hypoxaemia. It is important to compare the comparatively long time taken for electroencephalographic changes to occur after smothering with the comparatively short latency in prolonged expiratory apnoea, in which severe hypoxaemia is extremely rapid in onset.<sup>8</sup> Thus unconsciousness and electroencephalographic changes from cerebral hypoxaemia are present after only 30 seconds in this latter condition, whereas in smothering around 60-70 seconds of complete airway obstruction was present before the associated changes were detected. This adds weight to the hypothesis that prolonged expiratory apnoea is associated with severe ventilatory-perfusion mismatch, probably resulting from widespread alveolar atelectasis.<sup>17,18</sup>

It was clearly crucial that both mothers should receive psychiatric treatment. It is difficult to know how much to believe of the histories given concerning their childhood, as so much deception was woven into their stories. Nevertheless, it may be relevant that both mothers reported severe physical abuse from their fathers during adolescence.<sup>19,20</sup> If this can be validated it may have important implications with regard to prevention, diagnosis, and treatment.

In conclusion smothering is a comparatively rare but dangerous and preventable cause of hypoxaemic episodes in infants and young children. Diagnosis by video camera surveillance produces unequivocal evidence, avoids the need for nursing and medical staff to enter into confrontation with the mother in court, and prevents the trauma of confronting the mother with an incorrect suspicion. Unequivocal evidence is crucial to the adequate protection of the child. Future studies may show that a specific pattern on multi-

channel recordings of physiological variables is pathognomonic of imposed apnoea, thus avoiding the need for video surveillance.

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# Third trimester placental grading by ultrasonography as a test of fetal wellbeing

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## Abstract

In a study of 2000 unselected pregnant women the development of a mature placental appearance (grade 3) on ultrasonography by 34-36 weeks' gestation, observed in 15% of cases, was associated with maternal smoking, low parity, low maternal age, and being white. These women had an increased risk of problems during labour and their babies had an increased risk of low birth weight, poor condition at birth, and perinatal death. The women were

randomly allocated to two groups: in one group the result of the placental grading was reported to the clinician responsible for care; in the second the result was noted but not reported. There was a significant decrease in the risk of perinatal death in the group where the grading was known. This reduction was responsible for a difference in the principal outcome index, a heterogeneous group of measures of mortality and morbidity, but this difference was not significant.

This study alone does not justify routine late scanning, and further, larger trials are required. Nevertheless, the results do provide a basis for the reporting of placental grading when ultrasound examination is performed during the third trimester.

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## Introduction

The appearance of the placenta on ultrasound examination changes progressively with advancing gestational age, but the speed of these changes varies from pregnancy to pregnancy. Grannum *et al* first

described four stages (grades 0-3) of placental development that they used to relate placental maturation to fetal pulmonary maturity.<sup>1</sup> Placental grading has only limited usefulness in this respect,<sup>2</sup> but other investigators later reported an association between grade 3 placental maturation and subsequent obstetric problems, in particular intrauterine growth retardation and fetal distress in labour.<sup>3,5</sup>

There were two objectives of this study. The first was to test the hypothesis that early placental maturation, possibly through a relation with maternal smoking, is a predictor of subsequent obstetric problems. The second was to investigate in a randomised controlled trial whether clinical action taken on the basis of placental grading improved perinatal outcome.

## Patients and methods

The design of the study was based on the ultrasound scanning programme that existed at Peterborough maternity unit. The policy was for all women booked for delivery in the hospital to have three routine scans. The first was performed in early pregnancy to confirm gestational age and to rule out multiple pregnancy or any fetal or maternal abnormality. The second and third scans were performed at about 30-32 weeks' and 34-36 weeks' gestation respectively. In these, fetal presentation, measurements of the head and abdominal circumference, exclusion of specific fetal abnormalities, liquor volume assessment, the position of the placenta, and (from 1982) placental grading were reported. It was also policy to report the grade of the placenta at any other ultrasonographic examination during the third trimester.

Women attending the scanning department during the last trimester of pregnancy were given a written description of the study. Provided that they had no objections to participating they were then randomly allocated to one of two groups. In the first group placental grading was reported to the obstetricians for all ultrasound examinations thereafter. In the second group the placenta was graded but the grading was recorded only for the purposes of the study and was not reported in the casenotes (other details of the examination were reported as usual). Once entered in the study the women remained in their allocated group for all subsequent scans. The 1:1 randomisation was arranged in balanced blocks of varying size. The procedure for allocation was organised by a research assistant who was not concerned with the scanning or the clinical care of the participants. Each recruit was first allocated a trial number. A correspondingly numbered, sealed, opaque envelope (prepared in Oxford) was then attached to the casenotes and later opened by the ultrasonographer to show the trial allocation. Details of the placental grading were not made available for any women in the second group. Otherwise the clinical management of all women in the trial was left entirely to the obstetrician responsible for care and no attempt was made to standardise the clinical response to early placental maturation.

A standardised system was used for ultrasonographic placental assessment.<sup>1</sup> The grading was based on the appearance of the bulk of the placenta rather than the edges. All scans were performed by two experienced midwife ultrasonographers. They had a high level of agreement in their grading of placentas: in a series of 36 women who were independently assessed by both examiners there was agreement in all but one case, which was graded 0 by one and 1 by the other. The final trial size of 2000 was dictated by a change of staff in the scanning department. A newly promoted ultrasonographer did not have sufficient experience to grade placentas reliably as judged by a low level of agreement with an experienced ultrasonographer (JP) when a series of placentas was assessed by both independently.

The observational data of the study refer to the 1468 pregnant women who were scanned at 34 to 36 weeks' gestation. The predictive properties of grade 3 placental appearance at this stage of pregnancy for five prespecified

measures of outcome were expressed in terms of sensitivity, specificity, predictive values, and odds ratio, with the 95% confidence interval of the odds ratio calculated using Miettinen's method.<sup>6</sup> The birth weight for gestational age standards used were those of Secher *et al.*<sup>7</sup>

The main hypothesis tested in the randomised controlled trial was that knowledge of the placental grade would lead to clinical action that reduced the number of babies (who were not lethally malformed) who (a) died between trial entry and one week after delivery; or (b) had Apgar scores of less than 4 at one minute or less than 7 at five minutes; or (c) were admitted to the special care nursery. If the true prevalence of this combination of measures of adverse outcome was 8%, a trial of this size had a 65% chance of a significant result ( $\alpha=0.05$ ) if the real effect was a reduction by a third; the power was 85% if the true reduction was by 40%. The  $\chi^2$  and Student's *t* tests were used where appropriate.

## Results

### PLACENTAL GRADE 3 MATURATION AT 34-36 WEEKS

Of the 2000 women studied, 1468 (73%) were scanned at 34 to 36 weeks, 247 (12%) had a single scan at about 32 weeks, and the remainder were scanned once before 34 weeks and then for a second time after 36 weeks (almost invariably at 37 weeks). A grade 3 placenta at 34-36 weeks, observed in 15% of cases, was found to be significantly associated with low maternal age (age <20; 48 (22%) grade 3 v 134 (11%) grades 0-2); nulliparity 149 (67%) v 601 (48%); and being white 211 (95%) v 1113 (89%). The association with maternal smoking at booking was confirmed: 83 (37%) women with grade 3 placentas were smokers compared with 287 (23%) women with grades 0-2. A grade 3 placental appearance at 34-36 weeks was associated with an increased risk of meconium staining of the liquor, fetal distress in labour, low Apgar score, low birth weight, and perinatal death (table I). Secondary analyses showed that the association with low birth weight reflected both increased risk of preterm delivery (odds ratio 1.7, 95% confidence interval 0.9 to 3.0) and increased risk of low birth weight for gestational age (odds ratio 1.3, 95% confidence interval 0.8 to 2.0).

### THE RANDOMISED CONTROLLED TRIAL

The 2000 subjects were randomly divided into two equal sized groups. The mean gestational age at entry—and therefore at the first scan—was 31.7 weeks in the first group (placental grading reported to the clinician) and 31.8 in the second group. Randomisation produced groups which were also comparable in other important respects (table II).

Table III shows the clinical management of the trial groups. The main response to the report of early placental maturation seems to have been oestrial estimation. Despite the fact that induction of labour was less common in the first group, delivery tended to occur earlier. This primarily reflected a tendency for spontaneous labour to occur earlier in this group and a high rate of induction in the study population after 41 completed weeks. A caesarean section performed before labour had started and induction of labour were in fact more common in this group before 41 completed weeks. Meconium staining and no visible liquor were both more common in the second group, where the clinician did not know the placental grading ( $p<0.025$ ), and this was only partly explained by the difference between the trial groups in gestational age at delivery.

Table IV shows the neonatal outcome. Seventy one babies in the first group fulfilled one or more of the criteria of the prime measure of outcome compared with 83 in the second group. This estimated reduction in risk of 14% was not significant (95% confidence intervals 38% reduction to 16% increase). It did, however, largely reflect a difference in perinatal mortality (2 v 10 deaths not caused by lethal malformations,  $p<0.05$ ).

TABLE 1—Predictive properties of grade 3 placental maturation at 34 to 36 weeks' gestation

	No (%) in placental grade 0-2	No (%) in placental grade 3	Prevalence in total (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Odds ratio	95% Confidence interval	p Value
Meconium stained liquor*	93 (7.5)	32 (14.3)	(8.5)	26	86	14	93	2.1	1.4 to 3.2	<0.001
Emergency caesarean section for fetal distress†	29 (2.3)	14 (6.2)	(2.9)	33	85	6	98	2.8	1.5 to 5.1	<0.005
Apgar score <7 at 5 minutes†	16 (1.3)	7 (3.1)	(1.6)	30	85	3	99	2.5	1.0 to 5.9	<0.05
Low birth weight†	69 (5.5)	24 (10.6)	(6.3)	26	85	11	95	2.0	1.3 to 3.3	<0.025
Perinatal death†	3 (0.2)	4 (1.8)	(0.5)	57	85	1.8	99.8	7.5	2.1 to 26.6	<0.005

\* Placental grade 0-2=1245; grade 3=223.

† Rates are for babies and include twins. Placental grade 0-2=1256; grade 3=227.

Table V gives details of all the perinatal deaths subdivided by the Baird classification system.<sup>8,9</sup> The one case of unexplained death in the first group had a grade 3 placental appearance at 36 weeks. No special clinical action was taken on the basis of this information.

Of the (bottom) eight cases in the second group (table V), which might have been affected by knowledge of the placental grade, three had developed grade 3 appearance by 36 weeks and a further two had grade 3 placenta before term.

## Discussion

The two ultrasonographers who performed all the scans in this study showed near perfect agreement in their placental grading. Nevertheless, the subjective element of the test may result in important interobserver variation (as was our experience when a

TABLE II—Descriptive characteristics of trial groups at entry

	First group (placental grading reported to clinician) (n=1000)	Second group (placental grading not reported to clinician) (n=1000)
Maternal age (completed years) (mean (SD))	25.8 (5.5)	25.3 (5.1)
Nulliparity	487	509
Social class:		
1 and 2	233	241
3	287	258
4 and 5	454	484
Not known	26	17
Ethnic origin (non-white)	101	107
Smoker (when booked)	236	272
Consultant:		
A	341	350
B	334	328
C	325	322
Scan performed when women booked	950	960
Gestational age at entry (weeks) (mean (SD))	31.7 (1.0)	31.8 (1.0)
Pre-existing medical problems	137	155

TABLE III—Clinical management, labour, and delivery

	First group (placental grading reported to clinician) (n=1000)	Second group (placental grading not reported to clinician) (n=1000)
No of scans after entry:		
1	115	132
2	800	782
3	71	77
4-5	14	9
Oestriol estimation	268	208***
Cardiotocography performed:		
No	813	800
Mean (SE)	2.34 (0.08)	2.28 (0.08)
Antenatal admissions:		
No	312	304
Mean stay (SE)	2.52 (0.22)	2.33 (0.19)
Onset of labour:		
Spontaneous	717	701
Induced	218	237
Caesarean section before labour	59	55
Not known	6	7
Quality of liquor during labour:		
Clear	778	748
Meconium stained	70	101**
Blood stained	73	70
No liquor	16	21
Not applicable	52	48
Not known	11	12
Gestational age at delivery (weeks):		
<37	68	61
37-41	925	928
42+	1	4
Not known	6	7
Mean (SE)	39.09 (0.05)	39.22 (0.05)
Mode of delivery:	(n=1014)	(n=1011)
Normal vaginal	727	709
Instrumental	133	143
Emergency caesarean	73	81
Elective caesarean	62	59
Vaginal breech	13	12
Not known	6	7

\*\*p<0.025. \*\*\*p<0.01.

TABLE IV—Neonatal outcome

	No of babies	
	First group (placental grading reported to clinician) (n=1014)	Second group (placental grading not reported to clinician) (n=1011)
Apgar score:		
<4 at one minute	30	29
<7 at five minutes	12	25*
Intubation in delivery ward	20	17
Birth weight:		
<2500 g	72	75
<10th centile weight for gestational age	90	88
Mean (SD) (g)	3285 (521)	3305 (555)
Admission to special care nursery	48	60
Neonatal seizures	1	2
Antepartum stillbirth	0 (1)†	9 (3)†
Early neonatal death	2 (1)†	1 (0)†
Late neonatal death	0 (0)†	0 (0)†
Total perinatal deaths	2 (2)†	10 (3)*†
Subgroups of perinatal deaths:‡		
Congenital anomaly	2	3
Miscellaneous	1	1
Antepartum haemorrhage	0	2
Pre-eclampsia	0	2
Unexplained ≥2500 g	1	3
Unexplained <2500 g	0	2
Perinatal death and/or Apgar score <4 at one minute and/or Apgar score <7 at five minutes and/or admission to special care baby unit	71 (2)†	83 (3)†

\*p<0.05. †Figures in parentheses refer to deaths due to lethal malformations.

‡Baird and Thomson.<sup>8,9</sup>

new ultrasonographer joined the department). This may explain the prevalence rates different from ours reported from some hospitals<sup>10</sup> but not from others.<sup>11</sup> Clearly such variation could prejudice the usefulness of the test, and standardisation of interpretation is important before contemplating the introduction of this test into clinical practice.

For the purpose of assessing the predictive properties of early placental maturation we chose to concentrate on 34 to 36 weeks. Routine late ultrasound scans are commonly performed at this stage of pregnancy and elective delivery is a much safer option than it is before 34 weeks. Clinical action taken on the basis of a test result may alter the outcome against which the test is being compared and lead to an underestimate or overestimate of the test's performance. For this reason the intention had been to restrict the evaluation of the predictive properties of early placental maturation to the group in which the grading results had been withheld from the clinicians. In the event the results in the two trial groups in these respects were so similar that we chose to include all cases with scans in this gestational age period to give a larger sample size.

The study has confirmed the associations between early placental maturation and problems in labour, poor condition at birth, and low birth weight. As table I shows, a grade 3 placenta at 34-36 weeks is associated with an estimated increase of between 2 and 8 in the odds of having these conditions. None of the sensitivities are high, however, indicating that only a few babies with these conditions (with the possible exception of normally formed stillbirths) will show the signs of early placental maturation. Furthermore, low prevalence of the conditions coupled with specificities around 85% result in low predictive values of positive test results. In other words, although the chances of subsequent obstetric problems are apparently more than doubled in association with early placental maturation, only a few of these cases will actually develop a problem. This suggests that the finding of a grade 3 placenta at this gestation should lead to increased surveillance and supplementary tests of fetal wellbeing rather than to more definitive obstetric intervention.

The study also confirmed the association of early placental maturation with smoking in early pregnancy. Crawford *et al* observed differences between smokers and non-smokers in ultrasound placental texture as early as the second trimester and these persisted to delivery.<sup>12</sup> To put our findings another way, 23% of smokers developed grade 3 appearance between 34 and 36 weeks compared with 13% of non-smokers. The observed relation with

TABLE V—Details of the perinatal deaths

Case No	Baird class	Gestation (completed weeks)	Birth weight (g)	Scan performed (weeks of gestation)	Placental grading	Comments
<i>First group (placental grading reported to clinician)</i>						
1	Congenital anomaly	38	1991	32	2	Potter's syndrome, stillbirth
2	Congenital anomaly	39	3130	34	2	Spina bifida
3	Miscellaneous	38	2990	32	0	Good condition at birth. Neonatal infection. Sudden death on fourth day.
4	Unexplained ( $\geq 2500$ g)	39	3000	35	2	Poor condition at birth, ? birth asphyxia
				36	3	
<i>Second group (placental grading not reported to clinician)</i>						
5	Congenital anomaly	37	2100	32	2	Hydrocephaly, stillbirth, other abnormalities
6	Congenital anomaly	34	1580	35	3	Hydrocephaly, stillbirth
7	Congenital anomaly	39	2950	32	0	Spina bifida, stillbirth
8	Miscellaneous	39	2940	33	1	
9	Antepartum haemorrhage	34	2100	32	0	Good condition at birth. Sudden unexplained death on third day
10	Antepartum haemorrhage	39	3133	36	1	Abruptio placentae at 34 weeks, fresh stillbirth
				31	0	Bleeding on and off for the week before macerated stillbirth
				32	2	
				37	2	
				39	3	
11	Pre-eclampsia	32	1050	32	3	Proteinuric hypertension, small for gestational age on ultrasonography, macerated stillbirth
12	Pre-eclampsia	37	2820	30	1	Proteinuric hypertension, macerated stillbirth
				34	2	
13	Unexplained ( $\geq 2500$ g)	38	2800	30	0	Unexplained macerated stillbirth
14	Unexplained ( $\geq 2500$ g)	39	4430	36	3	
				32	1	Unexplained macerated stillbirth, no glucose tolerance studies performed
				37	1	
				40	1	
15	Unexplained ( $\geq 2500$ g)	39	4250	32	1	Unexplained macerated stillbirth
				37	2	
				38	3	
16	Unexplained ( $< 2500$ g)	38	1700	32	1	Recognised small for gestational age, reduced fetal movements, unexplained macerated stillbirth
17	Unexplained ( $< 2500$ g)	33	1200	35	3	Thought to be congenital abnormality at birth, not confirmed at necropsy, stillbirth with early maceration
				31	1	

ethnic origin was unexpected: only 8% of non-whites (predominantly from Asia) had grade 3 placental appearance at 34-36 weeks compared with 16% of whites. This was partly but not totally explained by the fact that the Asian women almost invariably did not smoke.

Before this study placental grading was already being used in clinical practice at Peterborough Maternity Hospital and no attempt was made to standardise the clinical response by the clinicians who knew the result. In fact the commonest response was additional oestriol estimations (table III).

Randomisation generated two trial groups that were comparable in important respects. The group where the clinician did not know the placental grading included slightly more young women who were in their first pregnancy, were of low social class, and were smokers. These minor imbalances, however, had no important effect on the conclusions drawn from the study. The trial was pragmatic and was superimposed on the ultrasound screening programme already in existence in the hospital.<sup>13</sup> Of the women recruited to the study, 1910 (96%) had been scanned early in pregnancy and 1753 (88%) followed the hospital policy and had two or more scans after entry to the trial.

The choice of a combination of measures of outcome on which to base the main hypothesis reflected the need for an index frequent enough to allow a reasonable chance of identifying a clinically plausible effect. Furthermore, even using this index the trial was not statistically very powerful. This is reflected in the fact that the trial's estimated reduction in bad outcome of 14% was not significant. The observed difference in the stillbirth rate was significant but was not a formal prior hypothesis and this secondary analysis therefore generates rather than tests a hypothesis. The observed fivefold risk reduction for normally formed perinatal deaths is certainly an overestimate of the true effect of this test (95% confidence interval of the relative risk 0.04 to 0.94). Nevertheless, the case review does suggest that some of the observed difference can be ascribed to the availability of the grading information.

This study alone does not justify routine scanning in late pregnancy. Further, larger randomised trials of placental grading

are required. Nevertheless, these results do provide a basis for recommending that placental grading should be one of the indices reported during ultrasound examination in the third trimester.

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